

**The Fragile Foundations of Regional Scientific Advantage?
The Impact of the US Administration Stem Cell Policy on the Geography of Scientific Discovery**

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I. Introduction

This paper evaluates the impact of restrictions on the use of embryonic stem cell lines in US Federally funded scientific research on the geography of scientific discovery. In order for localized knowledge spillovers to be translated into scientific leadership, researchers in close proximity to an original discovery must be able to exploit that discovery more rapidly and more intensively than more distant researchers. That is, local researchers must be able to take scientific advantage of a discovery more quickly than competitive researchers are able to catch up. Understanding the determinants of scientific leadership is important in its own right (Merton, 1957, Dasgupta and David, 1994; Nelson and Romer, 1996; Stephan, 1996; May, 1997), and is also significant for understanding the drivers of technological leadership (Nelson, 1993), the commercialization of knowledge in Pasteur's Quadrant (Murray and Stern, 2005), and, ultimately, in understanding the factors that contribute to long-term economic growth (Romer, 1990; Grossman and Helpman, 1991; Jones, 1995). In the specific case of stem cell research, examining the drivers of regional scientific leadership will also be important in anticipating the location of first advances in health care practices and outcomes that may be derived from stem cell science.

This paper exploits an exogenous shock to the process of step-by-step scientific discovery to assess the sensitivity of regional scientific agglomeration to a temporary revision in the knowledge production process. Specifically, we examine the impact of the Bush Administration's policy of limiting the scope of Federally-funded human embryonic stem cell research to a set of already existing stem cell lines on the rate of stem cell research progress in the United States and abroad.

II. Stem Cell Research: Promise and Policies

Over the past several years, research into the biological foundations of stem cells has been described by biologists as one of the most promising areas of scientific progress, and there have been rapid advances using both embryonic and non-embryonic stem cells, as well as human and non-human stem cell sources. Stem cells are initially undifferentiated cells that, ultimately, get transformed into cells with more specific functions. Among the many potential research agendas associated with stem cells, medical researchers hope to be able to understand and gain control over the process by which such cells become specialized. Doing so may help enable facilitate medical treatments in which stem cells could be used to replace other cells that have become diseased or malfunctional. In an optimistic scenario, discoveries based on stem cell research may contribute to medical treatments for severe conditions, such as diabetes and Parkinson's disease (NIH, 2001).

At least in the first few years after key discoveries enabled human embryonic stem cell research in the late 1990s, stem cell research had tended to be geographically localized, with a small number of locations and institutions accounting for a very large fraction of the overall discoveries. The laboratories of James A. Thomson and colleagues at the United States' University of Wisconsin were among the leaders in this area, as Thomson was the first researcher to demonstrate the ability to keep human embryonic stem cells alive *in vitro* (Thomson, 1998). Researchers in Israel, Australia, and the United Kingdom were among the early contributors to stem cell research, and historical accounts suggest that national policies associated with the use of human embryos played an important role in the configuration of relationships among stem cell scientists and in the affecting the set of researchers who entered this area of research (Vogel, 2005).

National policies became particularly relevant to stem cell research efforts in the United States when, in August, 2001, the Bush Administration enacted a policy that placed a subtle but substantive restriction on the freedom of Federally-funded researchers by limiting Federal funding with human embryonic stem cell lines to a small number of stem cell lines that had been developed prior to the date of the policy change. While researchers

were free to seek private funding, or to use these specific stem cell lines, qualitative research suggests that the policy placed significant restrictions on academic researchers dependent on Federal funding, and that adapting to the policy required a period of adjustment and exploration. This unexpected delay in the scientific productivity of those at the scientific frontier provided an opportunity for less well-positioned researchers to catch up and for equally well-positioned researchers to forge ahead during this period of adjustment.

The specific characteristics of this policy make for an unusually clean quasi-experiment, which we aim to exploit in order to evaluate its impact on the geography of science. Specifically, we view this policy as one that is plausibly exogenous from the standpoint of the science itself – that is the policy was not driven by US vs. foreign research productivity or progress. As well, the particular characteristics of the policy were likely quite unanticipated by scientists in the United States and abroad – there was substantial uncertainty about whether which presidential candidate would be elected, additional uncertainty about whether and when a Federal stem cell research policy would be enacted, and further uncertainty about the form that such a policy would take. It is therefore reasonable to believe that scientists' research decisions in the pre-policy period do not vary substantially between the United States and other countries in ways that are driven by the realized policy itself. As a consequence, we aim to conduct a differences-in-differences analysis to ascertain the impact of the Bush Administration policy on the rate and nature of stem cell research performed in the United States in comparison to other countries.

III. Data

Using an NIH report that was developed to inform discussion about the stem cell policy-making and that was released in during the summer prior to the announced policy, we have assembled a dataset of seminal stem cell articles published as of the time that policy was announced (NIH, 2001). Specifically, the NIH report lists 110 stem cell research papers that stem cell researchers and the NIH considered as seminal as of June 2001. For each article, we collected and characterize each of the citations received through the end of 2004. For each follow-on publication, we have information about the location and institutional affiliation of the researchers, as well as other publication and researcher characteristics.

When discussing the data, it is important to note that stem cell research can use either embryonic or adult cells that are derived from either human or animal sources. As a result, one can usefully characterize stem cell research into one of four types: (a) human embryonic; (b) human adult; (c) animal embryonic; or (d) animal adult. As the Bush Administration policy enacts restrictions only on human embryonic stem cell research, it may be possible to develop a control structure involving one or more of the other types of stem cell research. Our empirical examination focuses on whether the geographic pattern of human embryonic stem cell research after the Bush stem cell policy decision differs significantly from the pattern of regional agglomeration/dispersion realized by research into non-human and/or non-embryonic stem cell lines.

As a potential additional source of controls, we are in the process of gathering data on another substantial advance in cell biology that occurred in the late 1980s, RNA interference (RNAi). RNAi is a process that affects the strands of the RNA molecule and has been used, for example, as a technique to “knockout” genes in order to ascertain their particular functions. Like stem cell research, early advances in RNAi research were also substantially concentrated in the United States. By comparing the geography of this leading-edge area of cell biology (which was not directly affected by the Bush Administration policy) with that of stem cell research, we may gain additional understanding of the impact of the policy on regional scientific leadership.

IV. Preliminary Findings

Preliminary analysis of a subset of the data suggests that human embryonic stem cell research has experienced a rapid and significant shift in its level of geographic dispersion in the years 2002-2007 – a higher share of frontier discoveries take place outside of the United States. The increased international dispersion is also interesting in light of our preliminary comparison with the RNAi data. The RNAi data also evidence increasing international dispersion beginning in the year 2004. Overall, this evidence may be consistent with a particular impact of the Bush stem cell policy on stem cell research in the United States, but it may also be consistent with a more general international convergence in scientific research [Stephan, 2008].